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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Richard F Selden
Serial No.:	08/465,596
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Patent No.:	7,094,400
Issued:	August 22, 2006
For:	TRANSKARYOTIC IMPLANTATION
Examiner:	D. Crouch
Art Unit:	1632

Certificate of Mailing Under 37 CFR 1.8(a)
I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being deposited with the U.S. Postal Service on the date shown below with sufficient postage as First Class Mail, in an envelope addressed to: Attention: Certificate of Correction Branch, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

Dated: 10/26/06

Heather A. McLennand

REQUEST FOR CERTIFICATE OF CORRECTION
PURSUANT TO 37 CFR 1.322

Certificate
NOV 02 2006
of Correction

Attention: Certificate of Correction Branch
Commissioner for Patents
P.O. Box 1450
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Dear Sir:

Upon reviewing the above-identified patent, Patentee noted a typographical error by the Office that should be corrected.

In Claim 11, section f, line 51 is missing a comma after the word "autologous". Please correct the claim to read – autologous, --. A copy of the relevant page of the issued patent showing the correction in red is attached.

The comma appeared in the amendment filed January 27, 2006. Accordingly, no fee is required.

NOV - 3 2006

Transmitted herewith is a proposed Certificate of Correction effecting such amendment. Patentee respectfully solicits the granting of the requested Certificate of Correction.

Dated: October 26, 2006

Respectfully submitted,

By _____

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(Also Form PTO-1050)

UNITED STATES PATENT AND TRADEMARK OFFICE
CERTIFICATE OF CORRECTION

PATENT NO.	:	7,094,400
APPLICATION NO.	:	08/465,596
ISSUE DATE	:	August 22, 2006
INVENTOR(S)	:	Richard F Selden

It is certified that an error appears or errors appear in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

In Claim 11, section f, line 51, "autologous" should read -- autologous, --.

Certificate of Mailing Under 37 CFR 1.8(a)

I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being deposited with the U.S. Postal Service on the date shown below with sufficient postage as First Class Mail, in an envelope addressed to: Attention: Certificate of Correction Branch, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

Dated: 10/26/06 Signature: Heather A. McLennand (Heather A. McLennand)

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The above-described method may be used to facilitate the screening of resultant hybridoma cells for those which produce desired monoclonal antibodies. In conventional hybridoma technology, the hybridoma cells produced must be screened in order to identify those which produce antibody against a desired epitope. Such screening may be avoided in the present invention by introducing into the recipient animal transkaryotic cells which contain only a fragment of the antigen gene (and thus, are capable of producing only a fragment of the antigen molecule). By preselecting the gene fragment which is to be expressed by the transkaroytic cell, it is possible to limit the diversity of the hybridoma population.

EXAMPLE 16

Use of Transkaryotic Implantation to Identify Immunosuppressive Agents

If, in a transkaryotic implantation experiment, the implanted cells and the host animals are not syngeneic, the immunocompetent host will cause the rejection of the implanted cells. This rejection can be monitored by assaying for a product of the implanted cells, preferably hGH. When the transkaryotic animal is immunosuppressed, however, this rejection will be delayed or prevented, depending on the efficacy of the immunosuppressive regimen. In other words, the immunosuppressive regimen can be quantitatively evaluated by monitoring the levels and duration of serum hGH expression. Using this approach, several immunosuppressive agents have been studied, including cyclosporin, cyclophosphamide, dexamethasone, rabbit anti-mouse thymocyte antiserum, and anti-mouse thymocyte monoclonal antibodies. This technique is a straightforward, quantitative alternative to current methods of evaluation of immunosuppression.

While the invention has been described in connection with specific embodiments thereof, it will be understood that it is capable of further modifications and this application is intended to cover any variations, uses, or adaptations of the invention following, in general, the principles of the invention and including such departures from the present disclosure as come within known or customary practice within the art to which the invention pertains and as may be applied to the essential features hereinbefore set forth as as follows in the scope of the appended claims.

What is claimed is:

1. A method of transferring a plasmid containing a DNA sequence coding for a protein into a recipient subject comprising:

(a) transfecting autologous somatic cells in vitro with a plasmid containing a DNA sequence coding for a protein and which comprises a promoter by chemical or physical techniques to introduce the plasmid containing a DNA sequence coding for a protein into the cells;

(b) screening the resulting transfected somatic cells in vitro to select a cell, wherein the selected cell is stably transfected with the plasmid containing a DNA sequence coding for a protein so that the selected cell has the permanent capacity to direct expression of the DNA sequence coding for a protein; and

(c) cloning and expanding the selected somatic cell in vitro; and

(d) injecting the resulting transfected, isolated, autologous, screened, cloned, and expanded somatic cells into the recipient subject.

2. The method of claim 1, wherein the somatic cells are human cells.

3. The method of claim 2, wherein the human cells are selected from the group consisting of fibroblasts, myocytes, hepatocytes, kidney capsular cells, endothelial cells, epithelial cells of the gut, and pituitary cells.

4. The method of claim 2, wherein the plasmid contains a DNA sequence coding for a hormone or an enzyme.

5. The method of claim 2, wherein the plasmid contains a DNA sequence coding for human growth hormone.

6. The method of claim 2, wherein the plasmid contains a DNA sequence coding for human insulin.

7. The method of claim 2, wherein the transfection comprises calcium phosphate-mediated transfection, microinjection, electroporation, or DEAE-dextran transfection.

8. The method of claim 2, wherein the plasmid further comprises a regulatable promoter.

9. The method of claim 8, wherein the plasmid further comprises a selectable gene, and wherein the promoter is operably linked to the selectable gene.

10. The method of claim 2, wherein the screening step further comprises screening the resulting transfected somatic cells in vitro to select a cell possessing desired expression properties.

11. A method of transferring a plasmid containing a DNA sequence coding for a protein into a recipient subject comprising:

(a) providing autologous somatic cells;

(b) transfecting the somatic cells in vitro with a plasmid containing a DNA sequence coding for a protein and further comprising a promoter capable of functioning in the somatic cells, wherein the somatic cells are stably transfected with the plasmid containing a DNA sequence coding for a protein so that the somatic cells have the permanent capacity to direct expression of the DNA sequence coding for a protein upon induction of the promoter;

(c) screening the resulting transfected somatic cells in vitro to select a transfected somatic cell, wherein the screening comprises characterizing the transfected somatic cell with respect to expression and regulation of the DNA sequence coding for a protein by assaying for translation of mRNA into protein;

(d) cloning and expanding, in vitro, the transfected and screened somatic cell selected in step (c) to form the 10^5–10^{10} transfected, screened, cloned, and expanded somatic cells,

(e) combining the 10^5–10^{10} transfected, screened, cloned, and expanded somatic cells with a physiologically acceptable buffer or carrier; and

(f) injecting the resulting transfected, isolated, autologous, screened, cloned, and expanded cell preparation into the recipient subject.

12. The method of any one of claims 2 or 11, wherein the transferred plasmid contains a DNA sequence coding for human growth hormone.

13. The method of any one of claims 2 or 11, wherein the transferred plasmid contains a DNA sequence coding for insulin.

14. The method of any one of claims 2 or 11, wherein the plasmid containing a DNA sequence coding for a protein integrates into the chromosome of the selected cell.

15. The method of any one of claims 2 or 11, wherein the plasmid containing a DNA sequence coding for a protein replicates as an extrachromosomal plasmid.

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